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Results From an Expanded Cohort Phase 1 Study Published in the New England Journal of Medicine Demonstrate a Majority of Patients With ALK-Positive Advanced Non-Small Cell Lung Cancer Responded to Crizotinib (PF-02341066)

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First-in-Class ALK Inhibitor Rapidly Advanced to Phase 3 Development

"While this is a Phase 1 study, the high response rates observed in patients with ALK+ NSCLC who received crizotinib suggest that we may be one step closer to the development of"

(BUSINESS WIRE)--Pfizer Inc. (NYSE: PFE) announced today the publication of data showing that 57 percent of *ALK*-positive advanced non-small cell lung cancer (NSCLC) patients treated with crizotinib (PF-02341066), an investigational oral anaplastic lymphoma kinase (ALK) inhibitor, had either a complete (one patient) or partial (46 patients) response to treatment. Data from 82 patients in this Part 2 expansion cohort of the Phase 1 study were published in the October 28 issue of the *New England Journal of Medicine*.(1)

"It is gratifying to learn of responses like those seen in our study of crizotinib (PF-02341066), especially when you consider that most patients had already received two or more therapies by the time they entered the trial," said Dr. Eunice Kwak, MD, Ph.D., department of medicine, Harvard Medical School, assistant in medicine, hematology/oncology, Massachusetts General Hospital and lead author of the study. "As we're discovering more about lung cancer, we have confirmed the fundamental need to test tumors for molecular changes, like the ALK fusion gene, so we can better identify the patients who may benefit from certain treatments."

Updated results from this study were also recently presented at the 35th Congress of the European Society for Medical Oncology (ESMO) in Milan, Italy, reporting on 113 patients and preliminary median progression-free survival (PFS) data of 9.2 months.(2)

Study A8081001 is a 2-part Phase 1 open-label, multi-center study evaluating crizotinib (PF-02341066), in patients with solid tumors.(3) The Part 2 expansion cohort from study A8081001 is evaluating the safety and response of crizotinib (PF-02341066) in patients with *ALK*-positive advanced NSCLC treated with a dose of 250 mg twice daily.(1)

Crizotinib (PF-02341066) is a first-in-class compound that inhibits the anaplastic lymphoma kinase, or ALK.(4) ALK is believed to be a tumor-exclusive target that is a key driver of oncogenesis, or tumor development.(5) Approximately 3-5 percent of NSCLC tumors are ALK-positive.(4)

"The development of crizotinib is a testament to the benefits of collaboration and partnership, between industry and academia, with investigators from all over the world, including the United States, Japan, Korea and Australia, working together with the goal of discovering a more effective treatment for advanced NSCLC patients with few other options," said Dr. Mace Rothenberg, senior vice president of clinical development and medical affairs for Pfizer's Oncology Business Unit. "While this is a Phase 1 study, the high response rates observed in patients with ALK+ NSCLC who received crizotinib suggest that we may be one step closer to the development of "precision" or "personalized" cancer treatments that target specific genetic factors that drive certain tumors."

Pfizer is continuing to study crizotinib (PF-02341066) in an ongoing clinical development program,(6,7) and plans to submit crizotinib (PF-02341066) data in the first half of next year to the U.S. Food and Drug Administration (FDA) for regulatory review.

Additional trials of crizotinib (PF-02341066) include a randomized, Phase 3 open-label study, PROFILE 1007 (A8081007), evaluating the safety and anti-tumor activity of crizotinib (PF-02341066) versus standard of care chemotherapy in patients with previously treated *ALK*-positive advanced NSCLC.(5) PROFILE 1005 (A8081005) is a Phase 2 open-label, single-arm study of efficacy and safety of crizotinib (PF-02341066) in patients with *ALK*-positive advanced NSCLC who have received more than one line of prior chemotherapy.(6)

For more information on these clinical trials, please contact the Pfizer Oncology Clinical Trial Information Service at 1-877-369-9753 (US/Canada) or 1-646-277-4066 (international), via email at PfizerHPTrials@emergingmed.com or visit www.pfizercancertrials.com.

Study Results Published in the *New England Journal of Medicine*

In the Part 2 expansion cohort study which included 82 patients with *ALK*-positive advanced NSCLC, 57 percent (n=47)(95% CI 46%, 68%) of patients treated with crizotinib (PF-02341066) at a dose of 250 mg twice daily had either a complete or partial response to treatment. An additional 33 percent (n=27) met criteria for stable disease, including five unconfirmed partial responses. At eight weeks, the disease control rate (complete response (n=1) + partial response (n=46) + stable disease (n=24)) was 87 percent (n=71). Three patients with stable disease were not included in the disease control rate because their evaluation for response was outside a pre-specified timeframe.(1)

At the time of the analysis, 77 percent of patients (n=63) continued to receive treatment with crizotinib (PF-02341066). The median duration of treatment was 6.4 months, and follow-up is ongoing.

The most commonly reported all-grade adverse events associated with crizotinib included nausea (n=44), diarrhea (n=39), vomiting (n=36), and mild visual disturbances (n=34). Grade 3 ALT (alanine aminotransferase) and AST (aspartate aminotransferase) elevations occurred in four patients. One patient experienced a Grade 4 elevation in ALT and one patient discontinued treatment due to Grade 3 ALT increases. Tumors in the analysis were primarily of adenocarcinoma histology, and patients tended to be young, and were never or former light smokers. Ninety-three percent of patients (n=76) had received at least one prior therapy and five patients were treated in the first-line setting.(1) This Part 2 expansion cohort study of patients with *ALK*-positive advanced NSCLC, independent of the number of previous chemotherapies, followed the completion of the dose-escalation study which enrolled 37 advanced cancer patients with various tumors, including NSCLC, colorectal, pancreatic and inflammatory myofibroblastic tumor (IMT) tumors.(8)

These data were previously presented at the 2010 American Society of Clinical Oncology Annual Meeting.(7)

About Crizotinib (PF-02341066)

Crizotinib (PF-02341066) is a first-in-class compound that inhibits the anaplastic lymphoma kinase, or ALK,(3) and is representative of Pfizer's personalized medicine approach to cancer treatment. By inhibiting ALK, crizotinib (PF-02341066) blocks signaling in a number of cell pathways that may be critical for the growth and survival of tumor cells.(4) Crizotinib (PF-02341066) is also an inhibitor of c-MET (mesenchymal endothelial transition factor).(3)

About Non-Small Cell Lung Cancer

Lung cancer is one of the most common cancers worldwide.(9) NSCLC accounts for about 85 percent of lung cancer cases and remains difficult to treat, particularly in the metastatic setting. Approximately 75 percent of NSCLC patients are diagnosed late with metastatic, or advanced, disease, where the five-year survival rate is only 6 percent.(10,11) In addition, the current standard of care for advanced NSCLC demonstrates a response rate of only about 15 percent.(12) Approximately 3-5 percent of NSCLC tumors are *ALK*-positive.(4)

About Pfizer Oncology

Pfizer Oncology is committed to the discovery, investigation and development of innovative treatment options to improve the outlook for cancer patients worldwide. Our strong pipeline, one of the most robust in the industry, is studied with precise focus on identifying and translating the best scientific breakthroughs into clinical application for patients across a wide range of cancers, including breast, lung, prostate, sarcoma, melanoma, and various hematologic cancers. Pfizer Oncology has biologics and small molecules in clinical development and more than 200 clinical trials underway. By working collaboratively with academic institutions, individual researchers, cooperative research groups, governments, and licensing partners, Pfizer Oncology strives to cure or control cancer with breakthrough medicines, to deliver the right drug for each patient at the right time. For more information please visit www.Pfizer.com.

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DISCLOSURE NOTICE: The information contained in this release is as of October 27, 2010. Pfizer *assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.*

This release contains forward-looking information about a product candidate, crizotinib, including its potential benefits and the anticipated timing of its submission to the FDA, that involves substantial risks and uncertainties. Such risks and uncertainties include, among other things, the uncertainties inherent in research and development; decisions by the FDA and other regulatory authorities regarding whether and when to approve any drug applications that may be filed for such product candidate as well as their decisions regarding labeling and other matters that could affect its availability or commercial potential; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2009 and in its reports on Form 10-Q and Form 8-K.

(1) Kwak E et al. Anaplastic Lymphoma Kinase Inhibition in Non-Small Cell Lung Cancer. The New England Journal of Medicine. October, 27, 2010.

(2) ESMO Accepted Abstract # 366PD. Clinical Activity of Crizotinib (PF-02341066), in ALK-Positive Patients with Non-Small Cell Lung Cancer (NSCLC). Poster Discussion. Sunday, October 10: 12:30. David Ross Camidge – Presenter. 35th Congress of the European Society for Medical Oncology. Milan, Italy. October 8 – 12, 2010.

(3) ClinicalTrials.gov. A study of oral PF-02341066, A c-MET/Hepatocyte Growth Factor Tyrosine Kinase Inhibitor, in Patients with Advanced Cancer. Available at: http://clinicaltrials.gov/ct2/show/NCT00585195?term=A8081001&rank=1. Accessed August 31, 2010.

(4) Bang Y et al. Clinical Activity of the Oral ALK Inhibitor, PF-02341066, in ALK Positive Patients with Non-Small Cell Lung Cancer (NSCLC). Accepted Plenary Presentation at the American Society of Clinical Oncology 2010 Annual Meeting, June 4-8, 2010.

(5) Chiarle R, Voena C, Ambrogio C et al. The anaplastic lymphoma kinase in the pathogenesis of cancer. Nat Rev Cancer. 2008;8(1): 11-23.

(6) ClinicalTrials.gov. An Investigational Drug, PF-02341066 Is Being Studied Versus Standard Of Care in Patients With Advanced Non-Small Cell Lung Cancer With A Specific Gene Profile Involving The Anaplastic Lymphoma Kinase (ALK) Gene. 2010. Available at: http://clinicaltrials.gov/ct2/show/NCT00932893. Accessed August 23, 2010.

(7) ClinicalTrials.gov. An Investigational Drug, PF-02341066, Is Being Studied In Patients With Advanced Non-Small Cell Lung Cancer With A Specific Gene Profile Involving The Anaplastic Lymphoma Kinase (ALK) Gene. Available at: http://www.clinicaltrials.gov/ct2/show/NCT00932451. Accessed August 23, 2010.

(8) Bang Y et al. Clinical Activity of the Oral ALK Inhibitor, Crizotinib (PF-02341066), in Patients with ALK-positive Non-Small Cell Lung Cancer. Accepted Plenary Presentation at the American Society of Clinical Oncology 2010 Annual Meeting, June 4-8, 2010. Chicago, IL.

(9) American Cancer Society. Global Cancer Facts & Figures 2007. Atlanta, Ga: American Cancer Society: 2007.

(10) Reade CA, Ganti AK. EGFR targeted therapy in non-small cell lung cancer: potential role of cetuximab. Biologics. 2009; 3: 215–224.

(11) American Cancer Society. Detailed Guide: Lung Cancer (Non-Small Cell). Available at: \files\pressrelease_assets\pdf\003115-pdf.pdf. Accessed August 26, 2010.

(12) Huq S et al. Lung Cancer, Non-Small Cell: Treatment & Medication. Emedicine from WebMD. February 18, 2010. Available at: http://emedicine.medscape.com/article/279960-treatment. Accessed August 25, 2010.

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